

What is Claimed is:

1. An apparatus adapted for *in vitro* conditioning of cells prior to administration of the cells into tissue in a cell therapy, the apparatus comprising:
 - 5 a culturing module to host the cells and a culturing medium;
 - a cardiac electrical stimulator coupled to the culturing module;
 - a myocardial stress simulator coupled to the culturing module;
 - a biological treatment administration module coupled to the culturing module; and
 - 10 a controller coupled to the cardiac electrical stimulator, the myocardial stress simulator, and the biological treatment administration module, the controller adapted to control a delivery of one or more stimuli from one or more of the cardiac electrical stimulator, the myocardial stress simulator, and the biological treatment administration module.
- 15 2. The apparatus of claim 1, further comprising two or more electrodes, connected to the cardiac electrical stimulator and disposed in the culturing medium, to allow delivery of at least one electrical stimulus to the cells.
- 20 3. The apparatus of claim 2, wherein the electrical stimulator comprises a pacemaker.
4. The apparatus of claim 3, wherein the cardiac electrical stimulator comprises an electric field generator.
- 25 5. The apparatus of claim 1, wherein the culturing module comprises a deformable culturing substrate allowing the cells to be plated thereon.
6. The apparatus of claim 5, wherein the deformable culturing substrate is
30 made of silicone.

7. The apparatus of claim 6, wherein the myocardial stress simulator comprises a variable speed motor and a mechanical linkage coupled between the variable speed motor and the deformable culturing substrate, the variable speed motor and the mechanical linkage adapted to create a calibrated cyclic mechanical tension
5 upon the deformable culturing substrate.

8. The apparatus of claim 1, wherein the biological treatment administration module comprises one or more chemical dispensers adapted to release one or more biological stimulation agents into the culturing medium.
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9. The apparatus of claim 8, wherein the culturing module comprises a mixer adapted to create and maintain a homogeneous culturing medium.

10. The apparatus of claim 1, further comprising a user interface coupled to the
15 controller, the user interface including a use input accepting commands.

11. The apparatus of claim 10, wherein the controller comprises a memory circuit storing an instruction for an automated delivery of a sequence of one or more of electrical, mechanical, and biological stimuli.
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12. The apparatus of claim 11, wherein the user interface comprises a display screen.

13. The apparatus of claim 12, further comprising a monitor coupled to the
25 culturing module, the monitor adapted for observation of the cells in the culturing module.

14. The apparatus of claim 13, wherein the monitor comprises a microscope, coupled to the controller and the user interface, to allow observation of the cells on
30 the display screen.

15. A method for preparing donor cells for a cell therapy, the method comprising:
- disposing the donor cells in a culturing medium;
 - creating a cardiac electrical condition in the culturing medium, the cardiac
 - 5 electrical condition simulating an electrical condition of a myocardium;
 - creating a mechanical stress upon the donor cells, the mechanical stress simulating mechanical forces applied upon cardiac muscle cells in the myocardium;
 - and
 - introducing one or more exogenous agents to the culturing medium to
 - 10 change one or more biological properties of the donor cells.
16. The method of claim 15, wherein creating the cardiac electrical condition comprises delivering pacing pulses to the donor cells.
- 15 17. The method of claim 16, wherein delivering the pacing pulses comprises delivering pacing pulses having a pacing voltage of 0.1 to 10 volts and a pacing pulse width of 0.1 to 10 milliseconds.
18. The method of claim 16, wherein delivering the pacing pulses comprises
- 20 delivering the pacing pulses continuously for a predetermined duration.
19. The method of claim 18, wherein delivering the pacing pulses comprises delivering the pacing pulses continuously for 1 to 14 days.
- 25 20. The method of claim 16, wherein delivering the pacing pulses comprises delivering the pacing pulses for a predetermined duration interrupted by one or more non-pacing periods.
21. The method of claim 20, wherein delivering the pacing pulses comprises
- 30 delivering the pacing pulses at a duty cycle of 5 to 75 percent for 1 to 14 days.

22. The method of claim 15, wherein creating the cardiac electrical condition comprises applying an electrical field to the culturing medium.

23. The method of claim 22, wherein applying the electrical field comprises
5 applying a static electrical field having a strength of 1 to 100 volts per meter.

24. The method of claim 22, wherein applying the electrical field comprises applying the electrical field continuously for a predetermined duration.

10 25. The method of claim 24, wherein applying the electrical field comprises applying the electrical field continuously for 1 to 14 days.

26. The method of claim 22, wherein applying the electrical field comprises applying the electrical field for a predetermined duration interrupted by one or more
15 non-stimulating periods.

27. The method of claim 26, wherein applying the electrical field comprises applying the electrical field at a duty cycle of 5 to 75 percent for 1 to 14 days.

20 28. The method of claim 15, wherein creating the mechanical stress comprises subjecting the donor cells to a cyclic mechanical force so that the donor cells are cyclically stretched and relaxed.

29. The method of claim 28, wherein creating the mechanical stress comprises
25 extending the donor cells in at least one direction by approximately 5 to 20 percent of their length at a predetermined frequency of 0.25 to 2 hertz.

30. The method of claim 28, wherein creating the mechanical stress comprises applying the mechanical stress continuously for a predetermined duration.
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31. The method of claim 30, wherein creating the mechanical stress comprises applying the mechanical stress continuously for 1 to 14 days.

32. The method of claim 28, wherein creating the mechanical stress comprises
5 applying the mechanical stress for a predetermined duration interrupted by one or more non-stimulating periods.

33. The method of claim 32, wherein creating the mechanical stress comprises applying the mechanical stress at a duty cycle of 5 to 75 percent for 1 to 14 days.

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34. The method of claim 15, wherein introducing the one or more exogenous agents comprises introducing one or more of

a differentiation factor;

a growth factor;

15 an angiogenic protein;

a survival factor;

a cytokine; and

an expression cassette (transgene) encoding a gene product including one or more of an angiogenic protein, a growth factor, a differentiation factor, a survival
20 factor, a cytokine, a cardiac cell-specific structural gene product, a cardiac cell-specific transcription factor, a membrane protein, and an antisense sequence.

35. The method of claim 15, further comprising providing an image of the donors cells in the culturing module to allow observation by a user.

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36. A method for treating damaged cardiac tissue, the method comprising:
conditioning donor cells *in vitro*;

injecting the conditioned donor cells into a predetermined region in a heart;

and

30 delivering pacing pulses to the heart using an implantable pacemaker.

37. The method of claim 36, wherein conditioning the donor cells *in vitro* comprises applying one or more of an electrical stimulation, a mechanical stimulation, and a biological stimulation to the donor cells, wherein the donor cells are disposed in a culturing medium.

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38. The method of claim 37, wherein applying the electrical stimulation comprises delivering pacing pulses to the donor cells.

39. The method of claim 38, wherein applying the electrical stimulation further
10 comprise applying a static electrical field to the donor cells.

40. The method of claim 37, wherein applying the mechanical stimulation comprises cyclically deforming the donor cells.

15 41. The method of claim 40, wherein cyclically deforming the donor cells comprises stretching and relaxing the donor cells at a predetermined frequency.

42. The method of claim 37, wherein applying the biological stimulation comprises releasing chemical or biochemical agents to the culturing medium.

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43. A system for electrical therapy of cardiac tissue of a heart, at least a portion of the cardiac tissue administered with exogenous cells in a cell therapy, the system comprising:

an atrial lead, a first ventricular lead, and a second ventricular lead each
25 including one or more electrodes allowing for one or more of delivering electrical pulses and sensing electrical signals; and
a pulse generator including an interface for connections to the atrial lead, the first ventricular lead, and the second ventricular lead, a controller programmable for a plurality of pulse delivery modes, and a sense amplifier for sensing the electrical
30 signals from the atrial lead, the first ventricular lead, and the second ventricular

lead, wherein the pulse generator includes a selectable pacing mode for providing therapeutic electrical stimulation to enhance the cell therapy of the cardiac tissue.

44. The system of claim 43, wherein the therapeutic electrical stimulation
5 includes a VDD pacing mode having an atrioventricular delay which is short compared to an intrinsic atrioventricular delay of the heart.

45. The system of claim 44, wherein the atrioventricular delay is varied gradually over time.
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46. The system of claim 43, wherein the therapeutic electrical stimulation includes a DDD pacing mode having an atrioventricular delay which is short compared to an intrinsic atrioventricular delay of the heart.

47. The system of claim 46, wherein the atrioventricular delay is varied gradually over time.
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48. The system of claim 43, wherein the therapeutic electrical stimulation includes a biventricular pacing mode having a first atrioventricular delay and a second atrioventricular delay.
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49. The system of claim 43, wherein the therapeutic electrical stimulation includes a biventricular pacing mode having an atrioventricular delay and an interventricular delay.
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50. A method for enhancing cell therapy of cardiac tissue, the method comprising:
applying a pacing therapy using an implantable pulse generator to cardiac tissue administered with exogenous cell therapy comprising donor cells,
30 wherein the electrical therapy enhances one or more of engraftment, survival, proliferation, differentiation or function of the donor cells.

51. The method of claim 50, wherein the pacing therapy includes DDD-mode pacing with an atrioventricular delay which is relatively short compared to an intrinsic atrioventricular interval.

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52. The method of claim 51, wherein the atrioventricular delay is varied gradually over time.

53. The method of claim 50, wherein the pacing therapy includes biventricular
10 pacing with a first atrioventricular delay and a second atrioventricular delay.

54. The method of claim 50, wherein the pacing therapy includes biventricular pacing with an atrioventricular delay and an interventricular delay.

15 55. The method of claim 50, wherein the donor cells are conditioned *in vitro*.

56. The method of claim 55, wherein the donor cells are electrically stimulated *in vitro*.

20 57. The method of claim 55, wherein the donor cells are mechanically stimulated *in vitro*.

58. The method of claim 55, wherein the donor cells are biologically stimulated *in vitro*.

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59. The method of claim 50, wherein the pacing therapy is applied based on a level of activity.

60. The method of claim 59, wherein the pacing therapy is applied based on
30 certain times of day.

61. The method of claim 50, wherein the pacing therapy is applied during periods of relative inactivity.

62. The method of claim 61, wherein the pacing therapy is applied during sleep.

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63. The method of claim 50, wherein the pacing therapy is applied based on a level of stress.

64. A method comprising:

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delivering an electrical energy to a mammal subjected to cell therapy, wherein:

the cell therapy includes administration of exogenous cells into a tissue; and

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the electrical energy is delivered to the tissue hosting the exogenous cells to enhance one or more of engraftment, survival, proliferation and differentiation of the cells.

65. The method of claim 64, wherein delivering the electrical energy comprises delivering pacing pulses.

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66. The method of claim 65, wherein delivering the pacing pulses comprises applying VDD-mode pacing with an atrioventricular delay which is relatively short compared to an intrinsic atrioventricular interval.

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67. The method of claim 65, wherein delivering the pacing pulses comprises applying DDD-mode pacing with an atrioventricular delay which is relatively short compared to an intrinsic atrioventricular interval.

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68. The method of claim 64, further comprising conditioning the exogenous cells *in vitro*.

69. The method of claim 68, wherein conditioning the exogenous cells *in vitro* comprises one or more of applying an electrical stimulation, a mechanical stimulation, and a biological stimulation.